

ORIGINAL ARTICLE

Prospective cohort study showing changes in the monthly incidence of *Pneumocystis carinii* pneumonia

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Pneumocystis carinii pneumonia (PCP) remains a serious opportunistic infection in HIV infected individuals. Seasonal changes in climate are associated with changes within individual susceptibility to infection. The possibility of monthly variability in the incidence of PCP was therefore examined by means of a cohort study of a database of 8640 HIV infected individuals attending the Chelsea and Westminster Hospital. There were 792 cases of PCP diagnosed since 1985. A marked decline was observed in the incidence of PCP in mid-1992 coincident with the introduction of PCP prophylaxis. There was a further decline in 1996 after the introduction of highly active antiretroviral therapy. Despite no significant monthly variation in the mean attendance to clinic and CD4 count, both new and all cases of PCP were higher in January than in other months (15.9% and 14.5% of all cases, respectively). A correlation with low rainfall in January and new cases of PCP was observed. These data are consistent with an influence of climatic conditions on the presentation of PCP. The diagnosis of PCP is more common in winter months suggesting that this is a transmissible infection.

Pneumocystis carinii pneumonia (PCP) remains an important cause of morbidity and mortality in HIV infected individuals despite the advent of highly active antiretroviral therapy (HAART).¹ The probability of developing PCP rises markedly as the CD4 count falls below 200 cells/mm³ and it occurs predominantly in those who are undiagnosed or non-compliant with prophylactic medication.² Consequently, it has been thought that PCP is due to reactivation of latent organisms in the lung. Increasing evidence, however, suggests that *P. carinii* may be cleared in the immunocompetent host and that reinfection may be an important cause of PCP in the immunocompromised.³

It is well known that the incidence of certain viral and bacterial respiratory tract infections is subject to seasonal fluctuations.⁴ A few clinical investigators have recognised that the incidence of PCP may rise in colder months; however none of these studies have had sufficient numbers to examine this issue in detail.^{5–6} We therefore wished to study the incidence of this fungal infection among individuals infected with HIV-1 and relate this to month of diagnosis.

METHODS

The Chelsea and Westminster HIV cohort is one of the largest in Europe and we prospectively collect data on these individuals. HIV positive patients are seen at regular intervals for clinical assessment, trial follow up, immunological and virological assessments. All HIV patients who have attended the Chelsea and Westminster since routine prospective data collection started in 1985 were identified. This study focuses on those individuals who have received a new diagnosis of PCP since this time as recorded on the database. The data were analysed using Microsoft Excel and the Genmod procedure in SAS version 8.0. The temperature and rainfall for each month in the study were obtained from the meteorological office.⁷

RESULTS

A total of 8640 patients have been seen since January 1985 and a total of 792 new diagnoses of PCP have been made during this time, comprising a total of 9.2% of the clinic population. The median age was 44 (fig 1) and the median CD4 count

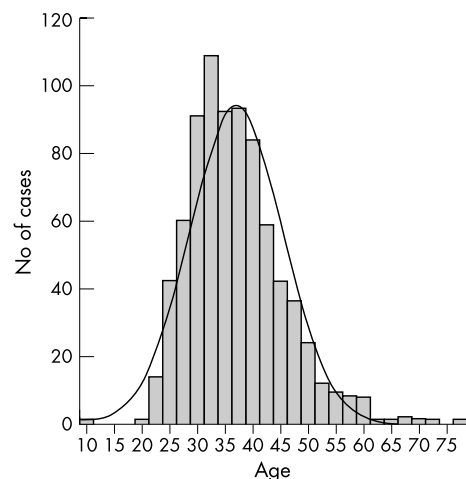


Figure 1 The age of patients diagnosed with PCP.

was 45 cells/mm³ (range 0–677). There were no statistically significant differences in the median CD4 counts or the number of individuals attending clinic each month (fig 2). The median CD4 count in the pre-HAART era, defined as before 1 January 1996 (the date at which HAART became routinely available in this institution) was 44 and the median CD4 count in the post-HAART era was 56 cells/mm³.

Figure 3 demonstrates that the number of new cases was highest in January (16% of all new cases). There was no correlation with peaks of rainfall (fig 3) or temperature (data not shown) for January, although an increase in rainfall and decrease in temperature was noted in the months preceding. The median rainfall in January was, however, lower than in all other months. The number of new cases decreased since the advent of PCP prophylaxis in 1992 and since HAART was

Abbreviations: HAART, highly active antiretroviral therapy; PCP, *Pneumocystis carinii* pneumonia

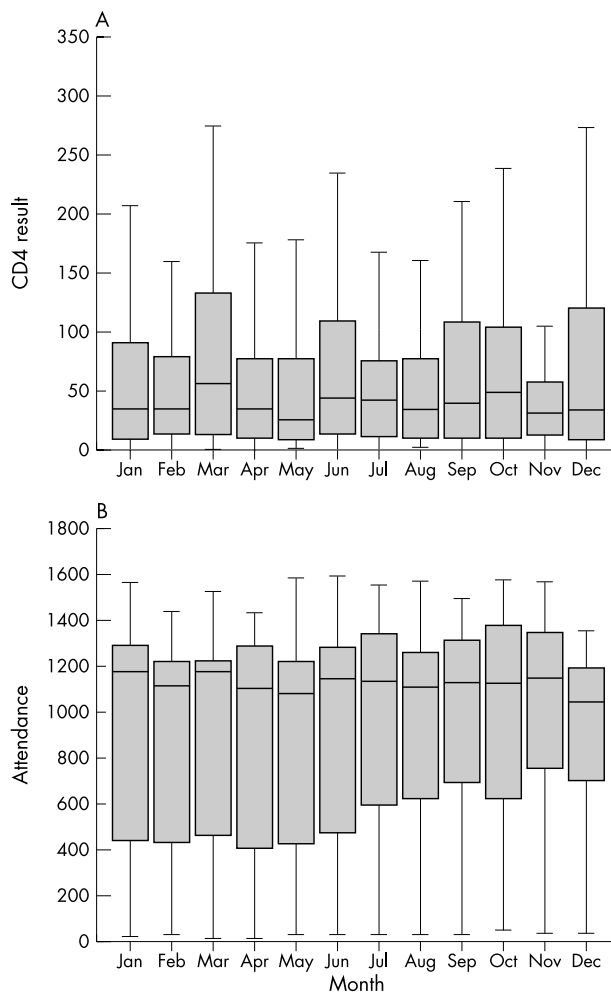


Figure 2 (A) CD4 count of patients per month (median and interquartile range). (B) Attendance at clinic each month.

introduced in 1996 (fig 4). The low number of cases observed between 1985 and 1989 is attributable to the low number of clinical attendees at that time (fig 5). There were no significant changes when results were calculated using all cases of PCP, as opposed to new cases only (data not shown).

DISCUSSION

Before the advent of antiretroviral therapy and prophylaxis against *P. carinii*, pneumonia due to this organism eventually occurred in 60%–80% of HIV infected adults in America and Western Europe.⁸ Longitudinal studies have recorded a dramatic decline in opportunistic infections, including PCP, attributed to effective antiretroviral therapy, increasing use of PCP prophylaxis, and increased awareness among health care professionals.^{9–10} Influenza, influenza-like illnesses, and bacterial pneumonia are more commonly diagnosed in colder months,^{11–12} and this cohort study of 792 HIV infected individuals with PCP shows that this diagnosis is also more common in January.

Recent studies have focused on the role of the climate in infection.¹³ For example, analysis of meteorological information obtained from satellite images of Gabon have shown that the climate changes from persistent, extremely dry conditions to colder, wetter weather over the two months before an outbreak of Ebola.¹⁴ In the United Kingdom the decrease in air temperature in winter is associated with an increase in morbidity and mortality for respiratory illnesses. For every degree Celsius decrease there is an increase in the number of winter deaths by around 8000. Approximately one

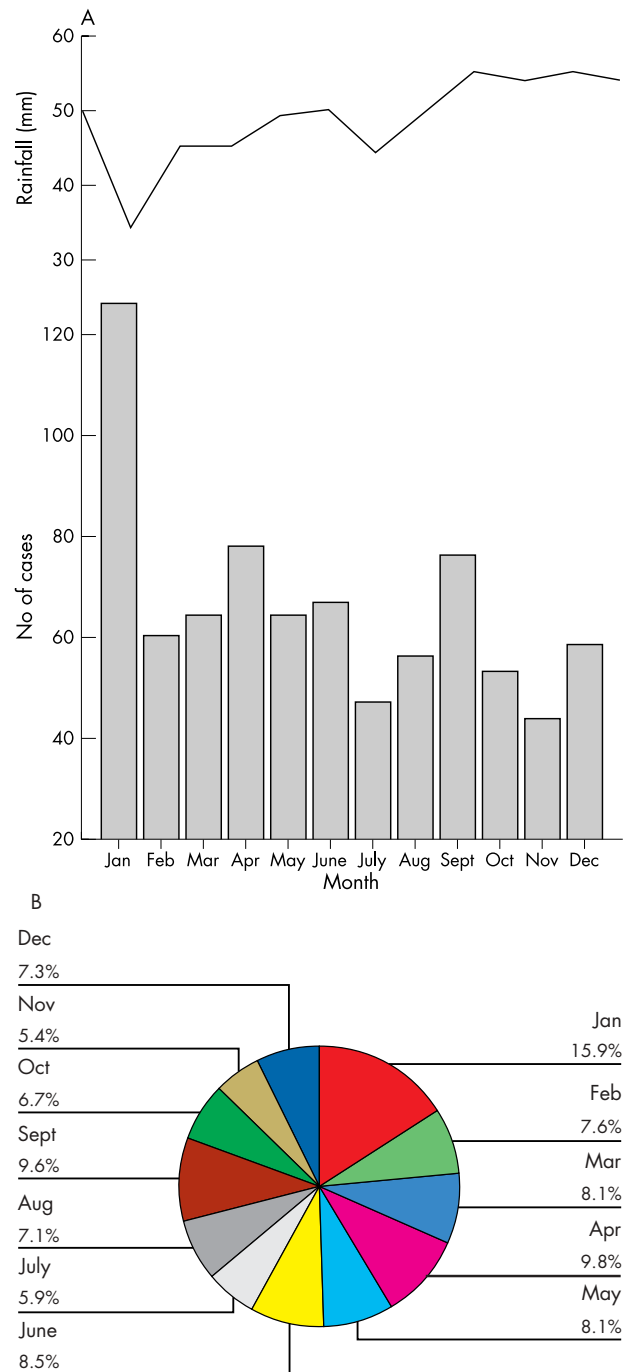


Figure 3 (A) New cases of PCP per month and median rainfall per month (mm). (B) Proportion of new cases of PCP each month.

third of this increase in mortality is related to respiratory illness and explanations often relate to increased crowding of susceptible individuals in colder months.¹⁵ It has also been suggested that inhalation of cold air causes cooling of the nasal and upper respiratory epithelium and that this reduction in temperature is sufficient to inhibit defences against infection including mucociliary clearance and leucocyte phagocytic activity.³ The contribution of these factors in relation to individual pathogens such as *P. carinii* has, however, yet to be ascertained. Interestingly, cyst forms of *P. carinii* in the field vole, *Microtus agrestis*, and in the common shrew, *Sorex araneus*, have been found in highest concentrations in late autumn (November).¹⁶ It is tempting to speculate that this cyst reservoir leads to a peak of cases of PCP as we observed here

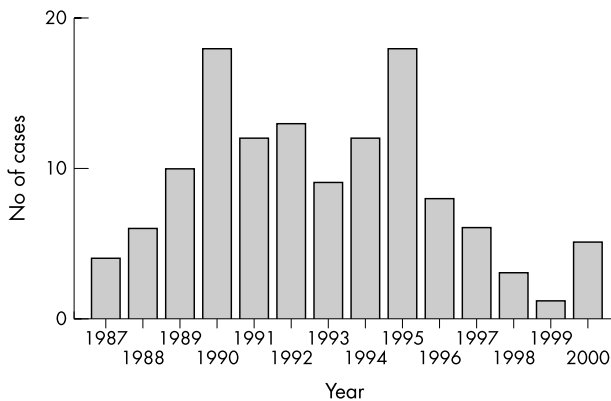


Figure 4 Total number of PCP cases per year presenting in January.

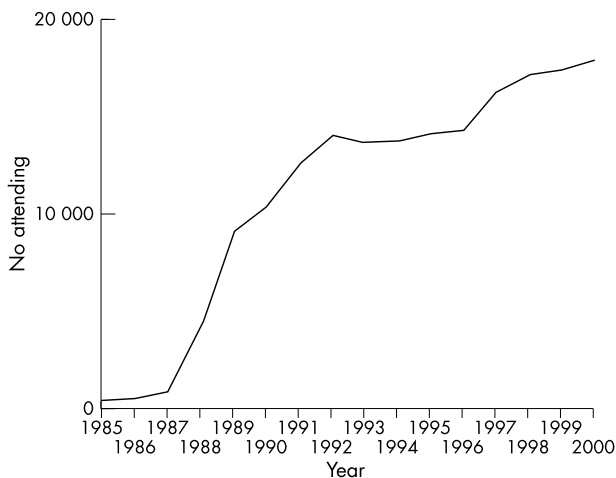


Figure 5 Number attending clinic each year.

in January, after an incubation period of several weeks in humans. Indeed it is well known that some individuals report symptoms such as a cough for several weeks before diagnosis.⁹

We found, as have others, that PCP has become a less common diagnosis in the years since HAART has become widely available. The rise in incidence of PCP in 1995 before the introduction of HAART (after PCP prophylaxis was introduced) is difficult to explain. Advances in our understanding of the molecular biology of *P. carinii* have raised questions regarding the possibility that certain strains may be more pathogenic than others, and that co-trimoxazole resistant strains may spread between individuals resulting in small outbreaks.^{17, 18} Our data suggest that *P. carinii* is transmissible and studies examining mitochondrial subunit ribosomal

rRNA genotypic differences from bronchoalveolar lavages of patients with separate episodes of PCP showed that different sequences were found in half, suggesting reinfection with a new strain of *P. carinii*.¹⁹

The monthly data shown here suggest that factors such as temperature may influence the spread of fungal spores into the environment, from which they may be inhaled and subsequently produce clinical disease in susceptible individuals.

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